

(1) Scientific Abstract

This phase I clinical protocol will evaluate particle mediated gene transfer of a novel melanoma vaccine consisting of cDNA for GP-100 given either alone or in combination with cDNA for GM-CSF. The use of the "gene gun" to directly deliver one or two genes into human skin represents an exciting treatment strategy for patients with melanoma. The cDNA for GP-100 encodes for an antigen that can stimulate T cell responses to melanoma, and the cDNA for GM-CSF encodes for a cytokine that can stimulate granulocytes and macrophages as antigen presenting cells. Available data support the safety of in vivo gene delivery with the "gene gun" as well as the strategy of immunotherapy with GP-100 either alone or in combination with GM-CSF. This study will obtain information about clinical toxicities associated with this treatment. In addition, important information about two separate dose levels of genetic vaccination will be obtained for each of the different treatment groups. The biological monitoring is an essential aspect of this protocol, and vaccine site biopsies will directly determine the expression of the GP-100 transgene following administration to human skin. In addition, ELISA assays will determine GM-CSF production at the vaccine biopsy sites. Immunohistochemical analyses will determine the nature of the lymphocytic infiltrate occurring at the vaccine site. The DTH analysis of HLA-A2 positive patients will determine whether an in vivo T cell response can be detected following this vaccine treatment. In addition, in vitro T cell assays will determine whether GP-100 reactive T cells have been stimulated with this protocol treatment. Thus, important information will be obtained in the biological monitoring to both interpret potential clinical activity seen in this study as well as help direct subsequent treatment plans with this gene based treatment. The planned biological monitoring will directly determine gene expression of the transgenes utilized in this study as well as determine immunological activity in patients following vaccination with cDNA for GP-100 either alone or in combination with GM-CSF. It is anticipated that this study will provide the foundation for subsequent Phase II evaluation of a melanoma vaccine consisting of cDNA for GP-100 given either alone or in combination with cDNA for GM-CSF.